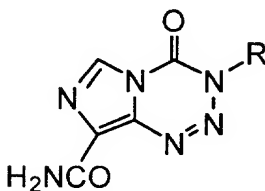


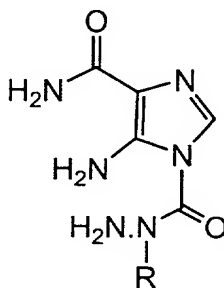
What is claimed is

1. A process for the preparation of a compound of the formula IA



IA

wherein R is an alkyl group having from 1 to 6 carbon atoms, which comprises reacting a compound of the formula II



II

wherein R is described above, with an oxidation/cyclization agent in the presence of an iodide, in an inert medium, under an inert atmosphere and at a temperature and for a time sufficient enough to produce a compound of the formula IA, wherein said iodide is soluble in said inert medium.

2. The process of claim 1 wherein R is an alkyl group having 1 to 4 carbon atoms.

3. The process of claim 1 wherein said oxidation/cyclization agent is selected from the group consisting of:

- a) periodic acid,
- b) iodine/potassium iodate,
- c) bromine,

- d) chlorine; and
- e) a reagent that oxidizes  $\text{NH}_2$  to  $\text{NZ}$ , where Z represents, Oxygen, (H, Hal), or  $\text{Hal}_2$ , and wherein Hal is chlorine, bromine or iodine.

5            4.        The process of claim 1 wherein said iodide is a quarternary ammonium iodide and said inert medium is an inert organic solvent.

             5.        The process of claim 4 wherein said iodide is selected from the group consisting of  $\text{Bu}_4\text{NI}$  and  $\text{KI}$ .

10           6.        The process of claim 4 wherein said inert organic solvent is selected from the group consisting of:

- a) an amide;
- b) an acyclic ether;
- c) a cyclic ether;
- d) an alkyl alkanoate wherein the alkyl group has 1 to 4 carbon atoms and the alkanoate grup has 2 to 4 carbon atoms;
- e) a halogenated hydrocarbon and
- f) mixtures thereof.

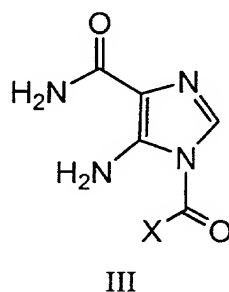
15           7.        The process of claim 6 wherein the organic solvent is selected from the group consisting of:

- a) DMF;
- b) t-butyl-methyl ether;
- 25        c) THF;
- d) acetonitrile;
- e) methylene chloride;
- f) toluene; and
- 30        g) mixtures of the above solvents,

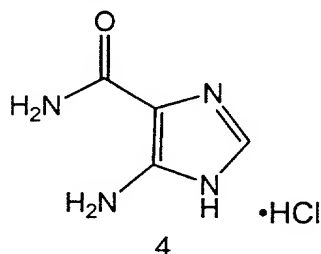
             8.        The process of claim 7 wherein the reaction takes place at a temperature of about  $(-)\text{20}^\circ\text{C}$  to about  $(+)\text{70}^\circ\text{C}$  and under a nitrogen atmosphere.

9. The process of claim 6 wherein:
- a) the organic solvent is a 50/50 mixture of THF/CH<sub>3</sub>CN;
  - b) the oxidation/cyclization agent is H<sub>5</sub>IO<sub>6</sub>;
  - c) the iodide is Bu<sub>4</sub>NI and
  - d) the reaction takes place at a temperature of about 0°C to about 60°C.

10. A process for preparing a compound of the formula III:



which comprises reacting a compound of the formula 4:



with a compound of the formula X-CO-Y, wherein each of X and Y is the same or different leaving group, to yield a compound of the formula III.

11. The process of claim 10 wherein X of said compound X-CO-Y is selected from the group consisting of

- a) phenoxy;
- b) 2-naphthyloxy and
- c) substituted phenoxy,

and wherein Y of said compound X-CO-Y is selected from:

- a) chlorine,
- b) bromine, or

c) iodine.

12. The process of claim 11 wherein the substituents on said substituted phenyloxy group are selected from the group consisting of:

- a) nitro;
- b) pentafluoro;
- c) chlorine;
- d) bromine;
- e) iodine, and
- f) combinations of the above.

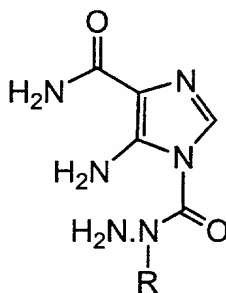
13. The process of claim 10 wherein said reaction of the compound of the formula 4 with a compound of the formula X-CO-Y is performed in the presence of an acid binding agent, in an inert organic solvent, under an inert atmosphere and at a temperature of about (-) 20°C to about (+) 50°C.

14. The process of claim 13 wherein said acid binding agent is a tertiary amine.

15. The process of claim 13 wherein the organic solvent is selected from the group consisting of

- a) an amide;
- b) an acyclic ether;
- c) a cyclic ether;
- d) an alkyl alkanoate wherein the alkyl group has 1 to 4 carbon atoms and the alkanoate group has 2 to 4 carbon atoms;
- e) a halogenated hydrocarbon, and
- f) mixtures thereof.

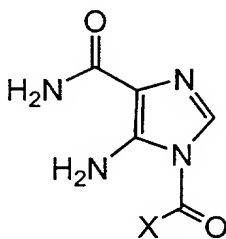
16. A process for the preparation of a compound of the formula II:



II

5

wherein R is an alkyl group having from 1 to 6 carbon atoms, comprising, reacting a compound of the formula III:



III

wherein X is a leaving group of the type that activates its adjacent carbonyl group towards nucleophiles, with an alkylhydrazine having from 1 to 6 carbon atoms.

15

17. The process of claim 16 wherein said alkylhydrazine is R-NH-NH<sub>2</sub>, wherein R is an alkyl group having 1 to 4 carbon atoms.

18. The process of claim 16 wherein the reaction takes place in an inert organic solvent selected from the group consisting of:

20

- a) a non-nucleophilic amine and
- b) an ether; and
- c) mixtures thereof.

19. The process of claim 16 wherein X is selected from the group consisting of:

- a) phenyloxy;
- b) 2-naphthyloxy and
- c) substituted phenyloxy, wherein the substituents are electron withdrawing.

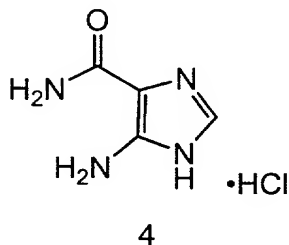
20. The process of claim 19 wherein said substituents are selected from the group consisting of:

- a) 2-nitro;
- b) 4-nitro;
- c) pentafluoro;
- d) chlorine and
- e) bromine.

21. The process of claim 17 wherein said alkylhydrazine is a 1-alkyl derivative of 5-amino-4-(aminocarbonyl)-1H-imidazole-1-carboxylic acid hydrazide wherein the alkyl group contains 1 to 6 carbon atoms.

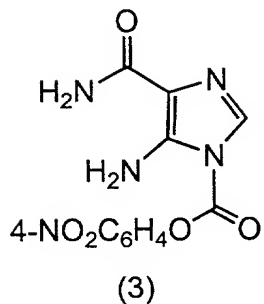
22. The process of claim 21 wherein said alkylhydrazine is 5-amino-4-(aminocarbonyl)-1H-imidazole-1-carboxylic acid 1-methylhydrazide.

23. The process of claim 14 wherein compound 4:

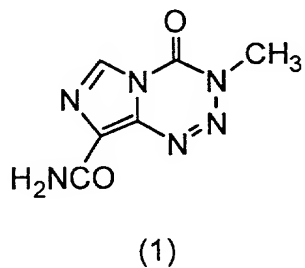


is reacted with 4-nitrophenyl chloroformate, in the presence of triethyl amine, said reaction taking place in methylene chloride solvent, under a nitrogen atmosphere and at a temperature of about (-)20°C to about (+) 50°C to yield compound (3):

21

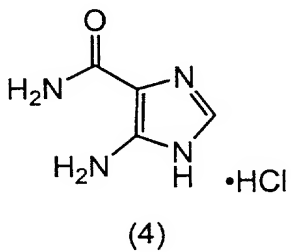


24. A process for preparing temozolomide (1):

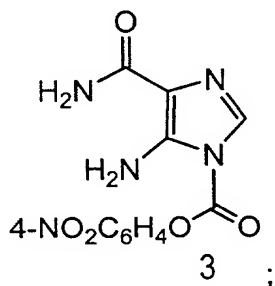


comprising:

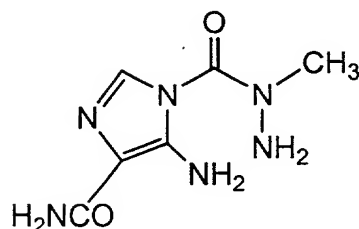
a) reacting compound 4:



with 4-nitrophenyl chloroformate in the presence of triethylamine in  $\text{CH}_2\text{Cl}_2$ , under a nitrogen atmosphere at about  $25^\circ\text{C}$  to obtain compound (3):



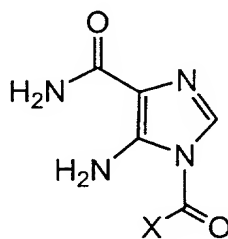
b) reacting compound (3) with methylhydrazine in DMF at about 0°C to obtain compound (2):



(2), and

c) reacting compound (2) with Bu<sub>4</sub>NI in a 50/50 mixture of THF/CH<sub>3</sub>CN, at a temperature of about (+) 60°C for a time of about zero to sixty minutes, followed by the cooling of the reaction mixture to about (+) 25°C and the addition of H<sub>5</sub>IO<sub>6</sub> and stirring for about 10 to about 60 minutes to obtain temozolomide (1).

25. A compound of the formula:



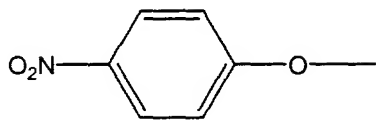
III

or an active ester thereof, wherein X is a leaving group of the type that activates its adjacent carbonyl group towards nucleophiles.

26. The compound of claim 25 wherein X is OH, said compound being 5-amino-4-(aminocarbonyl)-1H-imidazole-1-carboxylic acid.



5



28. The compound of claim 25 wherein X is  $-N(CH_3)-NH_2$ , said compound being 5-amino-4-(aminocarbonyl)-1H-imidazole-1-carboxylic acid-1-methylhydrazide.

28. The compound of claim 25 wherein X is  $-N(CH_3)-NH_2$ , said compound 5-amino-4-(aminocarbonyl)-1H-imidazole-1-carboxylic acid-1-hydrazide.